

PW Dkt. No. 021286/0272501

WHAT IS CLAIMED IS:

1. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof inhibits the binding of human CD40L to human CD40-human Fc fusion protein by less than about 28% when assayed in an in vitro ELISA assay under conditions wherein the antibody and human CD40L are added at equal concentrations (w/v).
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2. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof inhibits the binding of human CD40L to a human CD40-human Fc fusion protein by less than about 47% when assayed in an in vitro ELISA assay under conditions wherein the antibody and human CD40L concentration (w/v) are at a ratio of 2:1.
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3. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof substantially induces the proliferation of tonsillar B-cells in vitro without the addition of IL-4.
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4. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof substantially induces the proliferation of tonsillar B-cells in vitro without the addition of IL-4, wherein the proliferation efficiency is about 250% or greater than that induced by G28-5 antibody without the addition of IL-4, when the concentration of antibody is in the range of 0.01 μ g/ml to 1 μ g/ml.
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5. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof substantially induces the proliferation of tonsillar B-cells in vitro without the addition of IL-4, wherein the proliferation efficiency is about 250 to 800% greater than that induced by G28-5 antibody without the addition of IL-4, when the concentration of antibody is in the range of 0.01 $\mu\text{g}/\text{ml}$ to 1 $\mu\text{g}/\text{ml}$.
10. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof induces the proliferation of tonsillar B-cells in vitro, wherein the proliferation efficiency is about 62% or greater than that induced by G28-5 antibody, when the concentration of antibody is in the range of 0.01 $\mu\text{g}/\text{ml}$ to 1 $\mu\text{g}/\text{ml}$ in the presence of IL-4.
15. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof induces the proliferation of tonsillar B-cells in vitro, wherein the proliferation efficiency is about 62 to 87% greater than that induced by G28-5 antibody, when the concentration of antibody is in the range of 0.01 $\mu\text{g}/\text{ml}$ to 1 $\mu\text{g}/\text{ml}$ in the presence of IL-4.
20. 8. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof inhibits CD40L (1 $\mu\text{g}/\text{ml}$) mediated tonsillar B cell proliferation in vitro, wherein the inhibitory efficiency leads to about 50 to 95% or greater reduction in B cell proliferation when the concentration of the antibody is in the range of 0.01 $\mu\text{g}/\text{ml}$ to 10 $\mu\text{g}/\text{ml}$.
25. 9. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof inhibits CD40L

(1 μ g/ml) mediated tonsillar B cell proliferation in vitro, wherein the inhibitory efficiency leads to about a 85 to 95% or greater reduction in B cell proliferation when the concentration of the antibody is in the range of 0.1 μ g/ml to 10 μ g/ml.

5 10. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof inhibits CD40L (1 μ g/ml) mediated tonsillar B cell proliferation in vitro, wherein the inhibitory efficiency leads to about 80 to 95% or greater reduction in B cell proliferation when the concentration of the antibody is in the range of 0.01 μ g/ml to 10 μ g/ml.

10 11. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody or a functional fragment thereof inhibits CD40L (1 μ g/ml) mediated tonsillar B cell proliferation in vitro, wherein the inhibitory efficiency leads to about a 95% or greater reduction in B cell proliferation when the concentration of the antibody is in the range of 0.1 μ g/ml to 10 μ g/ml.

15 12. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody comprises the heavy chain variable region encoded by the nucleic acid sequence of SEQ. ID. 14 and the light chain variable region encoded by the nucleic acid sequence of SEQ ID 15.

20 13. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody comprises the heavy chain variable amino acid sequence of SEQ ID 16 and the light chain variable amino acid sequence of SEQ ID 17.

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14. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody comprises the heavy chain variable amino acid sequence and light chain variable amino acid sequence of the antibody produced by hybridoma F5-77.
- 5 15. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody is a recombinant antibody that comprises the heavy chain variable region and light chain variable region encoded by the nucleic acids isolated from hybridoma F5-77.
- 10 16. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody is selected from the group consisting of: a) an antibody comprised of the heavy chain variable region encoded by the nucleic acid sequence of SEQ ID 10 and the light chain variable region encoded by the nucleic acid sequence of SEQ ID 11, or b) an antibody comprised of the heavy chain variable region encoded by the nucleic acid sequence of SEQ ID 12 and the light chain variable region encoded by the nucleic acid sequence of SEQ ID 13.
- 15 17. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody is comprised of the heavy chain variable amino acid sequence and the light chain variable amino acid sequence of the antibody produced by hybridoma F1-102, F5-152, F2-103, F5-157, 72, or F4-465.
- 20 18. An anti-human CD40 antibody or a functional fragment thereof, wherein the antibody is a recombinant antibody that comprises the heavy chain variable region and the light chain variable region encoded by the nucleic acids isolated from hybridoma F1-102, F5-152, F2-103, F5-157, 72, or F4-465.
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19. An anti-human CD40 antibody or a functional fragment thereof, wherein the binding specificity to CD40 and its epitope thereof are the same as an antibody selected from claims 1 through 18.
20. The anti-human CD40 antibody or a functional fragment thereof of claims 1 through 19 wherein the heavy chain variable region and the light chain variable region of the antibody are the product of a human-derived antibody gene.
21. A pharmaceutical composition comprising at least one anti-human CD40 antibody or a functional fragment thereof selected from claims 1 through 20.
22. An isolated DNA molecule encoding the heavy chain variable amino acid sequence of SEQ ID 16.
23. The isolated DNA molecule of claim 16, wherein the DNA sequence comprises SEQ ID 14.
24. An isolated DNA molecule encoding the light chain variable amino acid sequence of SEQ ID 17.
25. The isolated DNA molecule of claim 16, wherein the DNA sequence comprises SEQ ID 15.
26. An isolated DNA molecule encoding the heavy chain variable amino acid sequence of the antibody produced by the hybridoma F1-102, F5-77, F5-152, F2-103, F5-157, 72, or F4-465.
27. An isolated DNA molecule encoding the light chain variable amino acid sequence of the antibody produced by the hybridoma F1-102, F5-77, F5-152, F2-103, F5-157, 72, or F4-465.

28. An isolated DNA molecule wherein the DNA sequence comprises SEQ ID 10, SEQ ID 11, SEQ ID 12, SEQ ID 13, SEQ ID 14 or SEQ ID 15.
29. An isolated polypeptide comprising a polypeptide having SEQ ID 16 or SEQ ID 17.
- 5 30. A host cell containing the nucleic acid selected from claims 22 through 28.